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Valvular Heart Disease/Cardiac Surgery

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AORTIC STENOSIS (AS)

Of 5,621 men and women ≥65 years of age in the Cardiovascular Health Study (1), 6% progressed from aortic sclerosis to AS over 5 years. Older age, male gender, and shorter height were predictors of progression to AS. Baseline C-reactive protein (CRP) concentration was not a predictor of calcific aortic valve disease at baseline or of its progression.

In a retrospective study of 818 patients (2), native AS progression could not be predicted by abnormalities in the seven markers of atherosclerotic risk.

High-grade AS valves (57 native valves and 24 bioprostheses) showed presence of endothelial progenitor cells, dendritic cells, and inflammatory cell markers (3). These changes were even more frequently found in bioprosthesis; cell density was higher in AS. These data point to a systemic origin of valvular cells and provide "novel insight" into mechanisms of aortic valve stenosis.

One-third of 216 patients age ≥75 years were denied aortic valve replacement (AVR) (4). Older age and depressed left ventricular ejection fraction (LVEF) were the characteristics most strongly associated with absence of surgery.

In the I-REVIVE trial (5), 16 patients had percutaneous implantation of an equine pericardial valve. Three patients died early. Among 11 implanted patients, 4 were alive at 6 months with normal valve function. The ReValving system using bovine pericardium for percutaneous valve replacement was initiated (6). A 21-patient feasibility study was also initiated.

MITRAL STENOSIS (MS)

Antibiotic prophylaxis: a meta-analysis was undertaken of 10 trials of young adults living on U.S. military bases from 1950 to 1961 (7). Antibiotic prophylaxis with a single injection of intramuscular (IM) penicillin for group A streptococcal infection was effective for preventing acute rheumatic fever with protective effect of 80% (fixed defect relative risk [RR] 0.20; 95% confidence interval [CI] 0.11 to 0.36); for a need to treat (NTT) number of 60, the marginal cost was $46.

Catheter balloon commissurotomy (CBC) for MS in 626 patients (8) showed the procedure was effective at a follow-up of 6.5 ± 2.5 years in those age ≥41 years, 42 to 53 years, 54 to 63 years, and in those age >63 years.

In 468 consecutive patients undergoing CBC for MS (9), the 5-, 10-, and 14-year event-free survival was 94 ± 1 %, 76 ± 9%, and 76 ± 9%. Mitral valve score by echocardiogram >8 and post-procedure mitral valve area (MVA) <2.0 cm^2 were predictors of restenosis ($p < 0.0002$ and $p < 0.002$, respectively).

MITRAL REGURGITATION (MR)

Degenerative (n = 20), rheumatic (n = 23), and control (n = 20) mitral valves were studied by electron microscopy and immunochemistry (10). Cellular proliferation and matrix production were shown to be important in the development of mitral valve disease. The severity of calcification correlated with higher levels of cellular proliferation and matrix production in calcified rheumatic valves as compared to degenerative mitral valves.

A total of 132 consecutive asymptomatic patients age 55 ± 15 years who had severe "degenerative" MR were seen from 1995 to 2002 and were followed until 2004. Mean ± SD for follow-up was 62 ± 26 months (11). There were four deaths: one sudden death in an 80-year-old; three deaths were unrelated to MR. Thirty-two patients had surgery for the following indications: symptoms, LVEF <60%, left ventricular end-systolic dimension ≥45 mm, pulmonary hypertension (pulmonary artery systolic pressure >50 mm Hg), or new onset of atrial fibrillation (AF). There was no operative mortality. At follow-up, LVEF was normal in 28 of 32 patients, the other 4 patients had mitral valve replacement (MVR) and coronary artery bypass graft surgery (CABG). Survival of the entire group at two years was 99 ± 1%, at four years 96 ± 2%, and at six and eight years was 91 ± 3%.

A retrospective review of the echocardiography database revealed 869 patients who had severe MR and normal LVEF (12). The mean age was 68 ± 17 years, 44% were men, LVEF was 66 ± 7%, diabetes mellitus was present in 19%, hypertension in 65%, and coronary artery disease (CAD) in 39% of patients. Mitral valve surgery was performed in 44%, and 42% of patients were on a beta-blocker. Use of a beta-blocker was associated with a significantly reduced mortality ($p = 0.002$), which remained unchanged after adjusting for age, gender, LVEF, CAD, diabetes, hypertension, and valve surgery. The independent beneficial effects of beta-blockers were seen in patients with CAD and no CAD and in patients managed both surgically and conservatively.

The outcome of 1,344 patients operated on between 1980 and 1995 for severe MR was analyzed by age: <65 years (n = 556), 65 to 74 years (n = 504), and ≥75 years (n = 284). At baseline, prevalence of severe symptoms, AF, CAD, "ischemic" MR, need for CABG, and creatinine level were

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higher in older versus younger patients (all $p < 0.002$) (13). Over the time periods of 1980 to 1983, 1984 to 1987, 1988 to 1991, and 1992 to 1995, operative mortality fell progressively, in the two older subgroups from about 23% to 27% to about 5%, the incidence of low-output state decreased from about 38% to 50% to ≥10% and the probability of mitral valve repair increased from approximately 30% to about 80% to 82% (all $p \leq 0.001$).

In patients with dilated cardiomyopathy, restrictive mitral annuloplasty (RMA) "effectively" restored MR without significant acute changes in baseline hemodynamics and left ventricular systolic function (14).

The EVEREST phase I clinical trial Evalve clip for percutaneous edge-to-edge mitral valve repair was performed in 20 patients, mean age 68 years, of which 75% were men (15). A partial clip detached in one patient, and surgery for MR was performed in two patients. Patients were discharged to home at an average time of 1.7 days. At 30 days' follow-up, the results were "encouraging." Posterior myocardial infarction (MI) was produced in six sheep and was compared to six control sheep. The percutaneous transvenous annuloplasty device was evaluated (16). The MR jet area, mitral valve tenting heights, and tenting area in all three commissures were significantly greater in chronic ischemic MR than in controls and were significantly reduced after coronary sinus-based annuloplasty.

TRICUSPID REGURGITATION (TR)

A total of 216 patients with functional TR were studied before and after tricuspid annuloplasty (17). Residual moderate TR was present in 15% and severe TR in 7.4% of patients. Multivariate analysis showed that age, tethering distance, and severity of preoperative TR were predictive of residual TR.

Severe symptomatic TR was associated with previous permanent pacemaker (PPM) or implantable cardioverter-defibrillator (ICD) (18). Forty-one patients with a mean age of 70 years (20 men; 21 women) had a normal tricuspid valve (TV) apparatus at surgery and 14 had dilated TV. The PPM lead TV perforation was found in 7, entanglement in TV leaflet or chordae in 4, impingement of the TV leaflets in 16 patients; adherence to the valve was seen in 14 patients. These findings were suspected in only 5 of 41 patients by preoperative transthoracic echocardiography and 4 of 13 patients in preoperative transesophageal echocardiography.

A total of 193 patients underwent MVR for rheumatic valve disease, of whom 57 also underwent tricuspid annuloplasty (TAP) (19). Of 21 patients (10.9%) who developed TR, mitral prosthetic valve function was normal. Severe TR developed in 11 of 35 (28.2%) patients who initially had severe TR. Despite successful TAP, the severity of TR at time of mitral valve surgery was the most important factor for prediction of severe TR after surgery.

Tricuspid valve replacement provided more complete elimination of TR than did annuloplasty (20). Right ventricular function was reduced after TVR, whereas it was preserved after annuloplasty.

Fifty-two patients underwent TV repair for functional TR (grade ≥3) due to annular dilation with three-dimensional ring annuloplasty for TR (Edwards MC^3 system) (21). At six-month follow-up, TR had a mean grade of 1.5 (range 0 to 2).

INFECTIVE ENDOCARDITIS (IE)

There was an unchanged pattern of IE. Over a period of 30 years (1970 to 2000), the population of Olmsted County, Minnesota, which consists largely of middle-class whites with an "extremely" low prevalence of intravenous (IV) drug abuse, was evaluated (22). The incidence of IE was relatively unchanged, and the leading causative organism was *Streptococcus viridans*.

In a multicenter, international study of prosthetic valve endocarditis (PVE), 355 patients were studied. Surgical treatment was utilized in 148 patients (41.6%), median time to surgery was 12 days, and 207 patients (59.4%) were treated medically (23). In-hospital mortality in the two groups was 24.3% and 22.7%, respectively ($p = 0.729$), and was "strongly related" to *S. aureus* infection and to the occurrence of cerebrovascular events with a trend toward improved survival with surgery. Surgery for complicated PVE resulted in a similar in-hospital survival rate as for uncomplicated PVE without surgery.

SURGERY

Postoperative AF occurred in 673 of 2,795 patients (24%) undergoing CABG (24). The incidence was higher in those with hypertension, chronic lung disease, cancer, and in subjects in New York Heart Association (NYHA) functional classes III/IV. Those who developed AF had longer stays in the intensive care unit and in the hospital, and also had a higher operative mortality (1.6% vs. 0.7%).

A prospective, randomized trial of four days of IV amiodarone was performed in 120 patients undergoing cardiac valve surgery (25). At four days, the incidence of AF was significantly lower in the amiodarone group (10% vs. 26%), but after drug discontinuation it was higher (37% vs. 19%).

A meta-analysis of 12 randomized trials of cardiothoracic surgery showed prophylactic amiodarone reduced the incidence of postoperative AF with an odds ratio (OR) of 0.47 (95% CI 0.39 to 0.57) but the differences of the effects on stroke and total hospital costs were not significantly different (26).

A prospective study of 648 patients undergoing cardiac surgery was performed at 14 VA Medical Centers (27). At baseline, 29.2% (189 of 648 patients) were depressed; they were younger; more were in NYHA functional classes III/IV, were on preoperative IV nitroglycerin or intra-aortic balloon pump, and had emergent surgery. Six-month mor-

tality was higher, 13.2% vs. 7.6%, in non-depressed patients ($p = 0.03$). On multivariable analysis, depressed patients had a higher mortality (OR 1.9, 95% CI 1.07 to 3.4; $p = 0.03$).

The 2001 Euro Heart Survey included 5,001 patients; 1,231 of these patients underwent valve surgery (28). The average age of the patients was 64 ± 13 years, with 43% in NYHA functional class I or II. The operative mortality for single-valve disease was 2.9%, for multiple-valve disease it was 6.5%, and for redo surgery it was 5.8%. The predictors of operative mortality were Euroscore ($p < 0.0001$), NYHA functional class ($p = 0.018$), and multiple versus single-valve surgery ($p = 0.021$).

A cohort of 240 consecutive asymptomatic or mildly symptomatic patients underwent aortic valve replacement (AVR) ± CABG between 1992 and 2004 (29). The operative mortality for isolated AVR (AS, n = 35; aortic regurgitation [AR], n = 82) was 0%; for AVR + CABG for AS (n = 9) it was 0%; and AR (n = 114) it was 1.6%.

In a randomized trial of surgical correction of permanent AF, 51 patients were randomized either to no cryoablation (control), Cox-Maze III surgery, or isolation of pulmonary veins (IPV) (30). At follow-up of 28.4 ± 14 months, the incidence of AF in the control group was 56.3%, whereas incidence of sinus rhythm in the IPV group was 88.9% and in the Maze group it was 84.6%.

Patients who had percutaneous coronary intervention followed by AVR (hybrid procedures; n = 20) versus CABG + AVR (standard; n = 114) had a statistically significant higher percentage of women, those who had previous cardiothoracic surgery, pulmonary hypertension, and peripheral vascular disease (31). The 90-day mortality was similar (5% vs. 4%); 1-year mortality was also similar (6% vs. 9%) as was 1-year MACE incidence was also similar (11% vs. 9%).

PROSTHETIC HEART VALVES

In a prospective study of 89 consecutive patients, mean age 67 ± 13 years, who had prosthetic heart valves, 77.5% of 69 ischemic cerebral events were shown by cranial computed tomography to be due to bleeding. The international normalized ratio was >5.0% in seven patients and <1.8 in four patients (32).

Of 131 explants for structural valve deterioration (SVD) in bioprosthetic MVR, the only predictor for SVD was younger age ($p < 0.001$) (33). Total cholesterol, high-density lipoprotein and low-density lipoprotein cholesterol, CAD, and creatinine levels were not predictors.

Finally, 15 porcine valves of similar annulus size were studied in a pulse duplicator at various flow rates to determine effect of increasing flow on bioprostheses of different stiffness (34). As flow rates were increased from 2.0 to 5.75 l/min, peak pressure gradient increased from 16 to 73 mm Hg ($p < 0.003$), the aortic valve area (AVA) ratio increased from 1.16 to 2.10 ($p < 0.003$). However, AVA at 2.0 to 5.75 l/min was 0.94 versus 0.99 (p = NS) and AVA at different flow rates ranged from 0.85 to 0.99.

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